



## DIAGNOSTIC ACCURACY OF CHROMOHYSTEROSCOPY IN DIAGNOSIS OF UNDIAGNOSED ENDOMETRITIS IN WOMEN WITH ABNORMAL UTERINE BLEEDING (AUB)

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Conflicts of Interest: Nil

### ABSTRACT:

**Introduction:** Chronic endometritis has been related to abnormal uterine bleeding but being a clinically silent disease, it is often asymptomatic. In absence of findings in TVS as well as in fluid hysteroscopy, endometrial dyeing using methylene blue helps in identifying abnormal areas and with HPE examination gives a better diagnosis of endometritis.

**Methods:** This study included 27 women with abnormal uterine bleeding in Department of Obstetrics and Gynaecology at SMS Medical College, Jaipur over a period of one year. All women underwent hysteroscopy and in the absence of any macroscopic abnormalities, chromohysteroscopy using 1% methylene blue dye. Biopsy was taken from light as well as dark stained areas. The histopathological results of these samples were compared and analysed in relation with differential staining pattern on chromohysteroscopic findings and diagnostic accuracy was calculated.

**Results:** Out of total 27 patients with AUB, 21 had DLS and 6 had FDS on chromohysteroscopy. 4(66.67%) patients of FDS were positive for endometritis on HPE. FDS had sensitivity, specificity, PPV and NPV as 100%, 91.30%, 66.67% and 100% respectively.

**Conclusion:** Chromohysteroscopy is a new, gainful and remunerative adjunct to hysteroscopy, for targeted sampling from correct site, worth pursuing to improve the diagnostic accuracy of endometrial biopsy.

**Keywords:** AUB, chromohysteroscopy, chronic endometritis.

### 1. Introduction

Endometrium is the inner most layer of uterus and endometritis is an infection and inflammation of the endometrial lining of the uterus.<sup>1</sup> This is a polymicrobial infection of the endometrium or decidua, usually results from an ascending infection from lower genital tract<sup>2,3,4</sup>.

From a pathologic perspective, endometritis can be classified as acute and chronic. Acute endometritis is characterised by presence of neutrophils within endometrial glands<sup>5,6,7</sup> while chronic variety is diagnosed by the presence of plasma cells within endometrium.

Clinically, it is often silent. Therefore, it is difficult to estimate its true prevalence in general population.<sup>8</sup> Sometimes clinically, it is diagnosed

by fever, abnormal uterine bleeding, dysmenorrhoea, dyspareunia,<sup>9</sup> infertility<sup>10,11</sup>, recurrent implantation failure<sup>12,13</sup> and recurrent miscarriages.<sup>14</sup>

Abnormal uterine bleeding (AUB) is characterised by bleeding at unexpected time or by excessive or decreased flow at time of expected menses. It is one of the most common clinical problems in gynaecology. Among uterine factors, chronic endometritis contributes to 3 - 10% of cases.

The diagnosis of chronic endometritis by means of two-dimensional transvaginal sonography (TVS) and hysteroscopy is difficult in the absence of macroscopic abnormalities. The criteria proposed by Cincinelli et al<sup>15</sup> to establish a hysteroscopic diagnosis of chronic endometritis are: - Hyperemia, Stromal edema and Micropolyps.

The histopathological diagnosis of chronic endometritis is based on the presence of: superficial stromal edema, increased stromal density, and inflammatory stromal infiltration predominated by the presence of lymphocytes and plasma cells<sup>16</sup>. The presence of a few or even a single stromal level plasma cell is also enough to settle the diagnosis of chronic endometritis.<sup>17</sup>

Accuracy of hysteroscopy and endometrial biopsy in diagnosing diffuse endometrial pathologies is not well established. Even visually directed biopsies can miss the lesions. Besides this, a normal appearance in conventional hysteroscopy does not assure integrity of endometrial cells.<sup>18</sup> Endometrial dyeing during conventional hysteroscopy using methylene blue is known as chromohysteroscopy. It can be used for the detection of endometrial changes that are not detected by the naked eye during hysteroscopy.<sup>19</sup> It seems like a new avenue worth pursuing for better diagnosis of unexplained endometrial pathologies.<sup>20</sup> Hence, the current study was done to evaluate the role of chromohysteroscopy in detecting endometritis in patients with normal TVS and hysteroscopy, using a safe, readily available and a cost effective, methylene blue dye.

## 2. Material and methods:

This was a hospital based comparative, cross sectional study carried out in the department of Obstetrics and Gynaecology at SMS Medical College, Jaipur over a period of one year. Ethical clearance was taken from Institutional Ethical Committee. Twenty seven women with abnormal uterine bleeding were included in our study after informed and written consent. Detailed history and clinical examination were done followed by baseline investigations. Chromohysteroscopy was

performed in all patients in proliferative phase, with normal TVS and hysteroscopic findings, guided biopsy was taken and sent for histopathology.

The uterine cavity was visualised as a whole for macroscopic abnormalities. After excluding all macroscopic abnormalities, 5 ml of 1% methylene blue dye was introduced through the hysteroscopic inlet. After five minutes of waiting, distending medium flow was continued again and endometrium was washed. Uterine cavity was then again visualised for staining pattern. Biopsies were obtained from light as well as dark stained areas and sent for histopathological examination in formalin.

## 3. Results:

The mean age of these women was  $29.18 \pm 7.29$  years in our study. Out of total 27 patients, 40.74% had only AUB, 44.44% of the cases had AUB along with infertility, while the rest 14.82% of the cases presented with AUB with failed IUI. 21(77.78%) showed diffuse light staining (DLS), while 6 (22.22%) had focal dark staining (FDS) on chromohysteroscopy and 4 (66.67%) patients of focal dark staining were positive for endometritis.

Out of 27 cases of AUB, occurrence of undiagnosed chronic endometritis was 14.81% on chromohysteroscopy, which were missed on conventional hysteroscopy (Table 1).

4 (66.66%) out of 6 cases with FDS were diagnosed with chronic endometritis on HPE, while no patient with DLS had chronic endometritis. FDS was 100% sensitive for detecting chronic endometritis. It had a specificity of 91.30% with a PPV of 66.67% and NPV of 100% (Table 2).

**Table 1: Distribution of AUB cases according to staining pattern**

Indication	Staining Pattern	No. of Cases	Endometritis on HPE
<b>AUB (11)</b>	DLS	8	0
	FDS	3	2
<b>AUB with Infertility (12)</b>	DLS	9	0
	FDS	3	2
<b>AUB with Failed IUI (4)</b>	DLS	4	0
	FDS	0	0
<b>Total (27)</b>	DLS	21 (77.78%)	0
	FDS	6 (22.22%)	4 (66.67%)

$$\chi^2 = 16.435 \quad d.f. = 4 \quad p = <0.001 \quad \text{Sig}$$

**Table 2: Association of HPE and Staining Pattern in Patients with AUB**

Staining pattern	No. of cases	Endometritis on HPE	Sensitivity	Specificity	PPV	NPV
<b>DLS</b>	21 (77.78%)	0	0.00%	8.70%	0.00%	33.33%
<b>FDS</b>	6 (22.22%)	4 (66.67%)	100%	91.30%	66.67%	100%
<b>Total</b>	27(100.00%)	4(14.81%)				

*p* value <0.001

#### 4. Discussion:

Conventional hysteroscopy is a gold standard test to diagnose endometrial pathologies but in the absence of macroscopic abnormalities chronic endometritis, which has subtle clinical manifestation, is difficult to diagnose. This led to birth of chromohysteroscopy.

In present study, mean age of total 27 patients was  $29.18 \pm 7.29$  years. 27 patients presented with complaint of abnormal uterine bleeding. , 40.74% had only AUB, 44.44% of the cases had AUB along with infertility, while the rest 14.82% of the cases presented with AUB with failed IUI. FDS was 100% sensitive for detecting chronic endometritis. It had a specificity of 91.30% with a PPV of 66.67% and NPV of 100%.

Methylene blue is an absorptive stain that is preferentially absorbed across epithelial cell membranes. Kucuk T et al<sup>20</sup> and Monsour H. et al<sup>21</sup> found that inflammatory cells had a higher uptake of methylene blue helping in diagnosis of unexplained endometritis.

Singh N et al (2013)<sup>22</sup> who did chromohysteroscopic guided endometrial biopsy in AUB patients. They observed that 4 (50%) out of 8 patients with focal staining had chronic endometritis. Thus proving a significantly higher diagnostic ability of focally stained tissue biopsy in detecting undiagnosed endometritis.

Abd El. Moneim A Saleh et al (2008)<sup>23</sup> did an analytical cross sectional study to evaluate the role of chromohysteroscopy in evaluation of endometrial pathology in women with perimenopausal bleeding. 100 patients were included in the study with no diagnosed

hysteroscopic endometrial abnormalities. According to the pattern of methylene blue staining, 60 patients showed focal dark and the remaining 40 showed diffuse light blue staining. The chromohysteroscopy procedure led to the diagnosis of 46 more new endometrial histopathologies missed by conventional diagnostic hysteroscopy. The overall diagnostic accuracy of chromohysteroscopy for detection of new histopathologies missed by the conventional hysteroscopy was calculated as sensitivity 93.2%, specificity 87.8%, PPV 91.6% and NPV 90% respectively.

Thus it was observed that on chromohysteroscopy, diffuse light blue staining strongly suggested a normal endometrium free of endometritis and focal dark blue staining signified areas of endometritis.

Chromohysteroscopy is thus a novel technique that has not been pursued much but it is a new avenue worth pursuing for better diagnosis of endometritis.

#### 5. Conclusion:

Conventional fluid hysteroscopy is a gold standard technique to detect intrauterine endometrial pathologies. Chronic endometritis, being a clinically silent disease, most often present with subtle clinical manifestation and is very difficult to diagnose in the absence of macroscopic abnormalities eg. hyperemia, micropolyps in fluid hysteroscopy. Endometrial dyeing during hysteroscopic procedure i.e. chromohysteroscopy, increases the accuracy of conventional hysteroscopy in detecting endometrial pathologies. Chromohysteroscopy is thus, a new, gainful and remunerative adjunct to hysteroscopy for targeted sampling from correct site, worth pursuing to

improve the diagnostic accuracy of endometrial biopsy.

## References

1. Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015 Jun 5. 64 (RR-03): 1-137.
2. Bayer-Garner Ib, Nickell JA, Korourian S. Routine syndecan-1 immunohistochemistry aids in the diagnosis of chronic endometritis. Arch Pathol Lab Med. 2004; 128: 1000-3.
3. McGill AL, Bavaro MF, You WB. Postpartum herpes simplex virus endometritis and disseminated infection in both mother and neonate. Obstet Gynecol. 2012 Aug; 120(2 Pt 2) : 471-3.
4. Onuigbo W, Esimai B, Nwaekpe C, Chijioke G. Tubercular endometritis detected through Pap smear campaign in Enugu, Nigeria. Pan Afr Med J. 2012; 11: 47.
5. Kitaya K. Accumulation of uterine CD16(-) natural killer (NK) cells: friends, foes, or Jekyll-and-Hyde relationship for the conceptus? Immunol Invest. 2008; 37(5) : 467-81.
6. Hardeman J, Weiss BD. Intrauterine devices: an update. Am Fam Physician. 2014 Mar 15. 89(6): 445-50.
7. Farley TM, Rosenberg MJ, Rowe PJ, Chen JH, Meirik O. Intrauterine devices and pelvic inflammatory disease: an international perspective. Lancet. 1992 Mar 28. 339 (8796) : 785-8.
8. Farooki MA. Epidemiology and pathology of chronic endometritis. Int Surg. 1967 Dec; 48(6) : 566-73.
9. Greenwood SM, Moran JJ. Chronic endometritis: morphologic and clinical observations. Obstet Gynecol. 1981 Aug; 58(2) : 176-84.
10. Kamiyama S, Teruya Y, Nohara M, Kanazawa K. Impact of detection of bacterial endotoxin in menstrual effluent on the pregnancy rate in in vitro fertilization and embryo transfer. Fertility and Sterility. 2004; 82 : 788-92.
11. Salim R, Ben-Shlomo I, Colodner R, Keness Y, Shalev E. Bacterial colonization of the uterine cervix and success rate in assisted reproduction: results of a prospective survey. Human Reproduction. 2002; 17: 337-40.
12. Cincinelli E, Matteo M, Tinelli R, Lepera A, Alfonso R, Indraccolo U, Marrocchella S, et al. Prevalence of chronic endometritis in repeated unexplained implantation failure and the IVF success rate after antibiotic therapy. Human Reproduction. 2015; 30: 323-30.
13. El-Toukhy T, Taranissi M. towards better quality research in recurrent implantation failure: standardizing its definition is the first step. Reproductive Biomedicine Online. 2006; 12: 383-5.
14. Kitaya K. Prevalence of chronic endometritis in recurrent miscarriages. Fertil Steril. 2011; 95: 1156-8.
15. Cincinelli E, Resta L, Nicoletti R, Zappimbulso V, Tartagni M, Saliani N. Endometrial micropolyps at fluid hysteroscopy suggest the existence of chronic endometritis. Human Reproduction. 2005; 20: 1386-9.
16. Smith M, Hagerty KA, Skipper B, Bocklage T. Chronic endometritis: a combined histopathologic and clinical review of cases from 2002 to 2007. Int J Gynecol Pathol. 2010 Jan; 29(1): 44-50.
17. Pitsos M, Skurnick J, Heller D. Association of pathologic diagnoses with clinical findings in chronic endometritis. J Reprod Med. 2009; 54 : 373-7.
18. Cincinelli E, De Ziegler D, Nicoletti R, Colafiglio G, Saliani N, Resta L, et al. Chronic endometritis : correlation among hysteroscopic, histologic, and bacteriologic findings in a prospective trial with 2190 consecutive office hysteroscopies. Fertil Steril. 2008; 89: 677-84.
19. Sano Y, Muto M, Tajiri H, Ohtsu A, Yoshida S. Optical/Digital Chromoendoscopy During Colonoscopy Using Narrow-Band Imaging System. Cochrane Library. Jul 2005; 7(1) : S43-S48.
20. Kucuk T and Safali M. "Chromohysteroscopy" for evaluation of endometrium in recurrent in vitro fertilization failure. J Assist Reprod Genet. 2008 Mar; 25(2-3): 79-82.
21. Mansour H, Mohamed MA. Value of endometrial dyeing in diagnosis of endometritis in the absence of macroscopic abnormalities during hysteroscopy. Middle

East Fertility Society Journal. 2011; 16 : 83-86.

22. Singh N, Singh B. Chromohysteroscopy - A new technique for endometrial biopsy in Abnormal Uterine Bleeding (AUB). Open Journal of Obstetrics and Gynecology. 2013; 3 : 11-14.

23. Abd El-Moneim A. Saleh, Mohamed E. Soliman, Mahmoud W et al. Role of chromohysteroscopy in evaluation of endometrial pathology in women with perimenopausal bleeding. Department of Pathology, Zagazig University. March 2012; 18(2).